

**Amendment and Response**

Applicant: Winthrop D. Childers

Serial No.: 09/878,108

Filed: June 7, 2001

Docket No.: 10008114-1 (H301.392.101)

Title: RAPID PHARMACEUTICAL COMPONENT SCREENING DEVICES AND METHODS

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**REMARKS**

The following remarks are made in response to the Office Action mailed December 14, 2004. Claims 2, 11-27, 29-30, 35, and 37 have been cancelled. Claims 1, 3-10, 28, 31-34, and 36-42 were rejected. Claims 37 and 39 have been objected to. With this Response, claims 36 and 38-41 have been amended. Claims 1, 3-10, 28, 31-34, 36, and 38-43 remain pending in the application and are presented for reconsideration and allowance.

**Claim Objections**

In the Office Action, claims 37 and 39 were objected to based on their manner of dependency and claim 37 was objected to based on its content. Applicant has canceled claim 37 and amended claim 39 to depend from claim 36, thereby obviating the objections. Accordingly, Applicant respectfully request withdrawal of the objections.

**Claim Rejections under 35 U.S.C. § 112**

The Examiner rejected claims 36-43 under 35 U.S.C. § 112, second paragraph, as being indefinite.

Applicant has amended claim 36 to refer to “the cartridge” as “the at least one consumable cartridge” throughout the claim. In addition, Applicant has amended claim 36 to recite “removably receiving into a test apparatus at least one liquid ejection device, the at least one liquid ejection device comprising at least one consumable cartridge including at least one chamber . . .”, thereby alleviating the source of the rejection regarding consumable cartridges.

Applicant has amended claim 39 to recite “removably associating the at least one chamber relative to the printhead”, thereby obviating the rejection.

Applicant has amended claim 41 to recite “the pharmacological effect” throughout the claim, thereby obviating the rejection.

With these changes, Applicant believes that the rejections under Section 112 is overcome and withdrawal of the rejection is respectfully requested.

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**Claim Rejections under 35 U.S.C. § 103**

In the Office Action, claims 1, 3-10, 28, 31-34, and 36-41 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Stylli et al., U.S. Patent No. 5,985,214 (herein Stylli) and Bullock et al., U.S. Patent No. 5,812,156 (herein Bullock).

Applicant's amended independent claim 1 specifies an automated method for analyzing substances containing cellular material.

Stylli discloses a system including, among other things, a storage and retrievable module and a sample distribution module. In the context of a sample distribution module, Stylli discloses a liquid handler which may comprise a plurality of nanoliter dispensers. See Stylli at Column 15, lines 39-68 and Column 16, lines 1-58. However, there are no Figures in Stylli illustrating the structure or features of the nanoliter dispensers and no Figures illustrating their relationship to other aspects of the modules of Stylli.

Accordingly, as detailed below, numerous aspects of Applicant's claimed method are not disclosed by Stylli (in addition to other differences described in previous Responses to Office Actions).

First, the nanoliter dispensers in Stylli do not include a memory storage device. Accordingly, the system in Stylli, particularly the nanoliter dispensers, do not enable capturing and maintaining information, via a memory storage device of at least one consumable cartridge, pertaining to the at least one potential pharmaceutically active agent or a function of the cartridge, as claimed by Applicant in claim 1.

Second, in Stylli, there is no electronic communication between a nanoliter dispenser and its reservoir from which it receives fluid, and therefore fails to disclose a method in which the consumable cartridge is removably received into the test apparatus to enable fluid communication and electronic communication between the at least one consumable cartridge and a drop-on-demand printhead, as claimed by Applicant in claim 1.

Third, the nanoliter dispensers in Stylli (and any reservoir associated with or forming a part of the nanoliter dispensers) are not consumable. Rather, the nanoliter dispensers in Stylli apparently form a permanent part of liquid handler and sample distribution module, and therefore are not consumable and are not removably receivable within a test system, as claimed by Applicant in claim 1. Moreover, the reservoirs described as part of or in cooperation with the nanoliter dispensers are not disclosed as being consumable.

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Accordingly, the nanoliter dispensers of Stylli do not describe or suggest removably receiving into a test apparatus at least one consumable cartridge for containing at least one potential pharmaceutically active agent, as claimed by Applicant in claim 1.

In Applicant's claimed method, the consumable cartridge allows disposal of the cartridge after depletion of agent from the chamber (e.g., reservoir) of cartridge – permitting a single use of the cartridge. This feature helps to maintain sterility of the test apparatus and avoids time-consuming cleaning operations of reservoirs, as would be necessary with the reservoirs of the nanoliter dispensers of Stylli. See Stylli at Col. 16, lines 52-58.

Accordingly, in Applicant's method, instead of washing out and rinsing the cartridge, prior to loading more agents/reagents into the cartridge, the empty cartridge is simply removed and a different cartridge containing an agent/reagent is inserted into the test apparatus for fluid communication with the printhead to enable faster resumption of testing.

Moreover, the feature of removably receiving the cartridge into the test apparatus permits removing the cartridge even prior to exhaustion of the agent from the chamber so that a different cartridge having a second agent can be inserted into the test apparatus.

Accordingly, one can switch agents being dispensed without having to perform a cleaning operation of the cartridge, and one can do so before the chamber (in fluid communication with the printhead) is emptied. Stylli fails to disclose such removable reception and/or consumability of its nanoliter dispensers, and particularly their reservoirs.

Applicant's specification describes the replaceable/consumable feature and the removable receiving of these cartridges into the test apparatus at page 6, paragraph 16; page 11, paragraph 39; page 13, paragraphs 44 and 45; and page 17, paragraph 60. Figures 2 and 3 also illustrate the ability to removably receive the replaceable/consumable cartridges.

Fourth, in Applicant's claimed method, the at least one consumable cartridge is removably received into the test apparatus, so that it is capable of already containing the at least one potential pharmaceutically active agent within the cartridge before the cartridge is removably received into the test apparatus.

In contrast, the nanoliter dispensers in Stylli (whether having solenoid valves or electrically sensitive volume displacement units) have reservoirs that hold liquids that are aspirated from an addressable chemical well (of the storage and retrieval module) (see Stylli Column 16, lines 11-15 and 29-33), so that the reservoirs are first empty and then contain a

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liquid for dispensing only after aspiration from the addressable chemical wells. The system in Stylli enables one mechanism (a sample distribution module) to aspirate fluids from a second mechanism (a storage/retrieval module) to enable fluids from at least 100,000 addressable chemical wells to be dispensed via the second mechanism, thereby enabling any one or more of an extremely large number of different fluids to be dispensed for use in screening chemicals and fluids.

For these reasons, Stylli fails to disclose Applicant's claimed automated method of analyzing substances containing cellular material, as specified in claim 1.

Bullock does not provide what Stylli lacks. Bullock is directed to a printer including a replaceable cartridge for housing a supply of consumable marking media, such as ink (Column 2, lines 21-22), and is in no way directed to dispensing potentially pharmaceutically active agents on a target cellular material, as claimed by Applicant. Accordingly, Bullock contains no suggestion or teaching to modify its printing system for use in a chemical identifying/screening device, such as in Stylli. No means is disclosed in Bullock for filling ink reservoir via aspiration from a source external to ink cartridge 20 of Bullock, as would be required if ink cartridge 20 of Bullock were substituted for the nanoliter dispensers of Stylli.

In addition, Stylli makes no suggestion to replace the nanoliter dispenser(s) with at least one consumable cartridge of the type claimed by Applicant. Moreover, Stylli is silent on any suggestions to modify the storage/retrieval module and/or to modify the sample distribution module to incorporate an at least one consumable cartridge that has its own chamber for holding fluid. In particular, no there is teaching in Stylli on how at least one consumable cartridge that has its own chamber (for holding fluid), as claimed by Applicant, would interface with aspirating equipment in communication with the at least 100,000 addressable chemical wells.

Substituting replaceable cartridges from Bullock for the dispensers in Stylli (which are filled from the 100,000 wells via aspiration) would be a major change, i.e., a difference of kind, rather than a slight change or obvious modification, i.e., a difference of degree. The apparent aim of Stylli is to make at least 100,000 different substances available for dispensing (through a much smaller number of dispensers, e.g., 98 dispensers). Placing a cartridge with a closed volume/cartridge, such as replaceable cartridge of Bullock, in Stylli would essentially make the vast library of liquids (100,000) in Stylli unavailable for use in

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testing since the cartridge would already be filled with a substance for dispensing. This arrangement would effectively render the collection of at least 100,000 liquids irrelevant. Alternatively, to make those same number of different liquids available for testing with in a modified system of Stylli, 100,000 cartridges would be required to achieve the same vast screening/testing function that was achieved in Stylli prior to modification by Bullock.

Accordingly, with no suggestions by either Stylli or Bullock on how to make the combination asserted in the Office Action, placing these two references (Stylli and Bullock) together would be performing hindsight reconstruction to force a combination not contemplated by either Stylli nor Bullock, thereby unfairly bypassing Applicant inventive accomplishment. In other words, it is unfair to use Applicant's claim as a starting point or guide to find features in different art areas (high volume chemical screening versus ink printer systems) and then conclude a lack of invention by Applicant when Applicant's claim was the source to link the two dissimilar references together. The combination is forced since it would practically frustrate the aim of Stylli to enable access to at least 100,000 fluids (via aspiration) for use in high-volume screening.

For these reasons, one skilled in the art would not combine Stylli and Bullock, and even if they were combined, one could not arrive at the invention of independent claim 1 based on the combination of Stylli and Bullock, as Bullock fails to cure the deficiencies of Stylli.

Accordingly, Stylli and Bullock, alone or in combination, fail to teach or suggest Applicant's claimed automated method of analyzing substances containing cellular material, and therefore Applicant respectfully submits that Applicant's amended independent claim 1 is allowable over Stylli and Bullock. Claims 3-10, 28, and 31-34 are also believed to be allowable as well based on their dependency from amended independent claim 1.

Applicant's independent claim 36 specifies an automated method for analyzing substances containing cellular material. For substantially the same reasons presented for the patentability of claims 1 and 36, Stylli fails to disclose claim 36. In particular, Stylli fails to disclose removably receiving into a test apparatus at least one liquid ejection device wherein the at least one liquid ejection device comprises at least one consumable cartridge including at least one chamber containing at least one potential pharmaceutically active agent, a

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memory storage device, and an electronically actuated drop-on-demand printhead in fluid communication with the chamber, as claimed by Applicant.

In addition, for substantially the same reasons presented for the patentability of claim 1, one skilled in the art would not combine Stylli and Bullock, and even if they were combined, one could not arrive at the invention of independent claim 36 based on the combination of Stylli and Bullock as Bullock fails to cure the deficiencies of Stylli.

For these reasons, Stylli and/or Bullock, alone or in combination, fail to teach or suggest Applicant's claimed automated method of analyzing substances containing cellular material, and therefore Applicant respectfully submits that Applicant's amended independent claim 36 is allowable over Stylli and/or Bullock. Claims 38 and 40 are also believed to be allowable as well based on the dependency of claims 38 and 40 from independent claim 36.

Applicant's independent claim 41 specifies an automated method for analyzing substances containing cellular material. For substantially the same reasons presented for the patentability of claims 1 and 36, Stylli fails to disclose claim 41. First, Stylli fails to disclose a replaceable cartridge that is removably received into a test apparatus and containing a potential pharmaceutically active agent. Second, Stylli fails to disclose that the replaceable cartridge, once removably received into the test apparatus, enables fluid communication and electronic communication with a drop-on-demand printhead, as claimed by Applicant in claim 41.

In addition, Stylli discloses a reaction module, referring to a second reagent dispenser and generally discloses having multiple dispenser with different reagents. However, at no time does Stylli disclosing dispensing a first defined volume onto target cellular material and then, based upon generated information about the pharmacologic effect of the first defined volume, interactively dispense a second defined volume onto the same target cellular material, as claimed by Applicant in claim 41. This claimed method is significantly different than generally identifying that many different reagents can be dispensed and that many different dispensers can be used.

Applicant again notes that the Office Action cites Stylli as disclosing a second dispenser, when Applicant's claimed method focuses on dispensing a second defined volume (of at least one potential pharmaceutically active agent) from the same at least one liquid

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ejection device that is used to dispense the first defined volume (of at least one potential pharmaceutically active agent), and that the second defined volume is dispensed in an interactive manner based on information generated from the test results of dispensing the first defined volume -- none of which is taught or suggested in Stylli.

The passages of Stylli cited in the Office Actions regarding a second reagent dispenser is limited to the context of the reaction module, which has a separate function and structure than either of the storage/retrieval module or the sample distribution module that has been extensively cited in the Office Actions. Stylli discloses that the reagent dispenser (of the reaction module) is of the type described in the Examples and non-specifically mentions that other reagent dispensers can be used. In the examples, Stylli alludes to several patents and publications as disclosing suitable reagent dispensers. See Stylli at Column 23, lines 20-60. Accordingly, Stylli on its faces does not disclose any details or structures of these reagent dispensers comprising a portion of the reaction module. A cursory review of the cited patents/publications within Stylli in the cited passage (Column 23, lines 20-60) reveals that they appear to disclose pipetting systems, stepper motors, piston/cylinder combinations, and pneumatic arrangements in order to dispense a fluid – none of them apparently disclosing Applicant’s claimed method in which a first defined volume is dispensed from an electronically actuated drop-on-demand printhead (as part of the at least one liquid ejection device) in fluid communication and electronic communication with a replaceable cartridge.

For these reasons, Stylli alone fails to disclose Applicant’s claimed automated method of analyzing substances containing cellular material, as specified in claim 41.

Bullock fails to cure the deficiencies of Stylli. For substantially the same reasons presented for the patentability of claims 1 and 36, Bullock should not be combined with Stylli and, even when Bullock is combined with Stylli, the combination fails to disclose, teach, suggest or make obvious claim 41.

Accordingly, Stylli and Bullock, alone or in combination, fail to disclose Applicant’s claimed automated method of analyzing substances containing cellular material, and therefore Applicant respectfully submits that Applicant’s amended independent claim 41 is allowable over Stylli and Bullock. Claims 42-43 are also believed to be allowable as well based on their dependency from amended independent claim 41.

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In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 3-10, 28, 31-34, 36, and 38-43 based on Stylli and Bullock under 35 U.S.C. §103(a).

**CONCLUSION**

In view of the above, Applicant respectfully submits that pending claims 1, 3-10, 28, 31-34, 36, and 38-43 are in form for allowance and are not taught or suggested by the cited references. Therefore, reconsideration and withdrawal of the rejections and allowance of claims 1, 3-10, 28, 31-34, 36, and 38-43 is respectfully requested.

No fees are required under 37 C.F.R. 1.16(b)(c). However, if such fees are required, the Patent Office is hereby authorized to charge Deposit Account No. 08-2025.

The Examiner is invited to contact the Applicant's representative at the below-listed telephone numbers to facilitate prosecution of this application.

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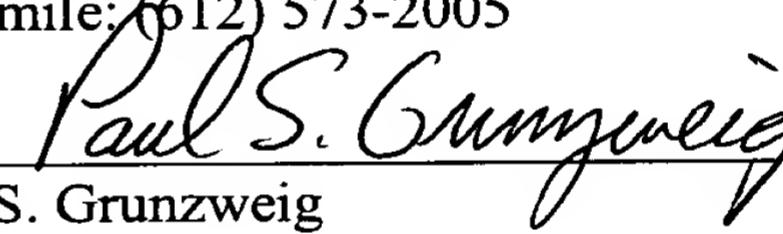
Respectfully submitted,

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**CERTIFICATE UNDER 37 C.F.R. 1.8:** The undersigned hereby certifies that this paper or papers, as described herein, are being deposited in the United States Postal Service, as first class mail, in an envelope address to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 14<sup>th</sup> day of March, 2005.

By Paul S. Grunzweig  
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